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Cartilage tissue engineering using a novel cell-derived extracellular matrix (ECM) scaffold in vitro and in vivo

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Purpose: In this study a cartilaginous tissue was fabricated by culture of rabbit articular chondrocytes seeded on a novel porous cell-derived ECM scaffold in vitro that was made from cultured porcine chondrocytes. Based on the in vitro results, the chondrocytes seeded ECM scaffold was implanted into rabbit osteochondral defects on the patellar groove to evaluate its feasibility as a reconstructive construct for cartilage restoration.
Methods and Materials: The chemical composition of the ECM scaffold was examined by HPLC following 2-D analysis and FT-IR assay. A cartilaginous tissue was first fabricated in vitro by culturing rabbit articular chondrocytes on the cell-derived ECM scaffold for 4 weeks. The neocartilages were analyzed by histological and chemical assays for GAG, collagen and DNA contents. In in vivo study, the cultured neocartilage tissue in vitro was implanted into the rabbit osteochondral defects on the patellar groove (5mm in diameter), and the repair of the cartilage was evaluated by gross observation, histological assays and ICRS score at 1 and 3 months post-surgery.
Results: The in vitro cultured tissues were observed as a white and smooth cartilage-like tissue by gross and histological staining such as Safranin O stain. In the rabbit study, the cartilage defects were filled with hyaline-like cartilage tissue, showing mature matrix and columnar organization of chondrocytes in experimental group at 3 months post-surgery. The ICRS histological scores were significantly increased over time.
Conclusions: In conclusion, our cell-derived ECM scaffold could be a promising supporting material for cartilage tissue engineering.

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In situ Tissue Engineering - cell-free regeneration of cartilage defects

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Purpose: Currently applied cartilage tissue engineering grafts are based on the implantation of chondrocytes. The objective of this study was the development of a cell-free cartilage tissue engineering graft that allows the in situ recruitment of mesenchymal stem cells (MSC) by chemoattractants and subsequent guidance of the progenitors towards formation of cartilage repair tissue.
Methods and Materials: Chemotactic activity of chemokines, synovial fluid (SF) and human serum was tested in 96-well chemotaxis assays. Chondrogenic differentiation was assessed by histological analysis and gene expression profiling after stimulating MSC with hyaluronan and SF in high-density cultures. Chemoattractants and chondroinductors were combined with poly-glycolic acid (PGA) scaffolds and were implanted into full-thickness articular cartilage defects of the sheep pre-treated with microfracture. Defects treated with microfracture served as controls.
Results: Distinct chemokines, like SDF1 and IL8, recruited MSC, and SF as well as human serum were potent chemoattractants. Chondrogenic differentiation of MSC upon stimulation with SF or hyaluronan was shown by the formation of a proteoglycan-rich tissue in vitro and the induction of typical chondrogenic marker genes like type II collagen and aggrecan. 3 months after implantation of the cell-free graft, histological analysis documented the formation of a cartilaginous repair tissue. Controls treated with microfracture, only, showed no formation of a repair tissue.
Conclusions: Here we report the development of the first cell-free in situ cartilage tissue engineering graft utilizing the migration and differentiation potential of mesenchymal progenitors. The cell-free cartilage graft is well suited for the treatment of cartilage defect after microfracture.